

Amendment to the specification:

Insert the paper copy of the Sequence Listing filed herewith following the Drawings.

Please amend the paragraph beginning at page 9, which starts with “*DNA sequence*”, as follows:

*DNA sequence (Factor X sequence shown in gray):*

GAC TCT AAG AAA GAC ATT TCG AAT GTT AAA AGT GAT TTA CTT TGC  
GCA TAC ACT ATA ACT CCT **ATC GAA GGT CGT** ACG CCT GCT CAA AAT  
AAT AAA GTA AAT CAT AAA TTA TTG GGA AAT CTA TTT ATT TCG GGA  
GAA TCT CAA CAG AAC TTA AAT AAC AAG ATT ATT CTA GAA AAG GAT  
ACC GTA ACT TTC CAG GAA ATT GAC TTT AAA ATC AGA AAA TAC CTT  
ATG GAT AAT TAT AAA ATT TAT GAC GCT ACT TCT CCT TAT GTA AGC  
GGC AGA ATC GAA ATT GGC ACA AAA GAT GGA AAA CAT GAG CAA ATA  
GAC TTA TTT GAC TCA CCA AAT GAA GGG ACT AGA TCA GAT ATT TTT  
GCA AAA TAT AAA GAT AAT AGA ATT ATC AAT ATG AAG AAC TTT AGT  
CAT TTC GAT ATT TAT CTT GAA AAA TAA (SEQ ID NO:5)

Please amend the paragraph beginning at page 9, which starts with “*Protein sequence*”, as follows:

*Protein Sequence:*

D S K K D I S N V K S D L L C A Y T I T P I E G R T P A Q N N K V N H K L L G N  
L F I S G E S Q Q N L N N K I I L E K D T V T F Q E I D F K I R K Y L M D N Y K I Y D A  
T S P Y V S G R I E I G T K D G K H E Q I D L F D S P N E G T R S D I F A K Y K D N R I I  
N M K N F S H F D I Y L E K Stop (SEQ ID NO:6)

Please amend the Table 1 beginning at page 12, as follows:

Table 1: Primers used for amplification of the SPEC gene and introduction of mutations or truncations

SPEC - N-terminal	CGGGATCCGACTCTCAAGAAAGACA ( <u>SEQ ID NO:7</u> )	
SPEC - C-terminal	CTGAATTCTTATTTCAAGAT ( <u>SEQ ID NO:8</u> )	
SPEC- Y15A	GATTTACTTGTGCATACAC ( <u>SEQ ID NO:9</u> )	GTGTATGCACAAAGTAATC ( <u>SEQ ID NO:15</u> )
SPEC- N79C	ATATTCTTGTCTCACAC ( <u>SEQ ID NO:10</u> )	TATAAGAAACAAGAGTGT ( <u>SEQ ID NO:16</u> )
SPEC- Y15C	GATTTACTTGTGCATACAC ( <u>SEQ ID NO:11</u> )	GTGTATGCACAAAGTAATC ( <u>SEQ ID NO:17</u> )
SPEC- R181Q	GAAGGGACTCAATCAGATATTTTGCT ( <u>SEQ ID NO:12</u> )	GACAAAATATCTGATTGAGTCCCTTC ( <u>SEQ ID NO:18</u> )
SPEC-(-20-90)	ATCGAAGGTCGTACGCCTGCTCAAATAATAAG ( <u>SEQ ID NO:13</u> )	ACGACCTTCGATAGGAGTTAGTGTAT ( <u>SEQ ID NO:19</u> )
SPEC- C27S	GATTATAAAGATTCCAGGGTAA ( <u>SEQ ID NO:14</u> )	TTACCCCTGGAATCTTATAATC ( <u>SEQ ID NO:20</u> )

Please amend the paragraph beginning at page 17, line 1, as follows:

Primary DNA sequences of the wild-type and the mutant form of SPE-C are detailed below:

*SPE-C wild type (from GenBank)*

**Streptococcus pyogenes pyrogenic exotoxin C gene, 5' end cds**

GACTCTAAGA AAGACATTTC GAATGTTAAA AGTGATTTAC TTTATGCATA CACTATAACT CCTTATGATT ATAAAGATTG CAGGGTAAT TTTCAACGA CACACACATT AAACATTGAT ACTCAAAAT ATAGAGGGAA AGACTATTAT ATTAGTTCCG AAATGTCTTA TGAGGCCTCT CAAAAATTAA AACGAGATGA TCATGTAGAT GTTTTGGAT TATTTTATAT TCTTAATTCT CACACCGGTG AGTACATCTA TGGAGGAATT ACGCCTGCTC AAAATAATAA AGTAAATCAT AAATTATTGG GAAATCTATT TATTCGGGA GAATCTAAC AGAACTTAAA TAACAAGATT ATTCTAGAAA AGGATATCGT AACTTCCAG GAAATTGACT TTAAAATCAG AAAATACCTT ATGGATAATT ATAAAATTAA TGACGCTACT TCTCCTTATG TAAGCGGCAG AATCGAAATT GGACACAAAG ATGGGAAACA TGAGCAAATA GACTTATTTG ACTCACCAAA TGAAGGGACT AGATCAGATA TTTTGCAAA ATATAAAGAT AATAGAATTA TCAATATGAA GAACTTTAGT CATTTCGATA TTTATCTTGA A (SEQ ID NO:1)

**Protein Sequence – wild type**

DSKKDISNVK SDLLYAYTIT PYDYKDCRVN FSTTHTLNID TQKYRGKDYY ISSEMSYEAS QKFKRDDHVD VFGLFYILNS HTGEYIYGGI TPAQNNKVNH KLLGNLFISG ESQQNLNNKI ILEKDIVTFQ EIDFKIRKYL MDNYKIYDAT SPYVSGRIEI GTKDGKHEQI DLFDSPNEGT RSDIFAKYKD NRIINMKNFS HFDIYLE (SEQ ID NO:2)

**SPEC- Y15A.C27S.N79C.R181Q**

GAACCTCTAAGA AAGACATTTG GAATGTTAAA AGTGATTTACT **TATG**CATA CACTATAACT  
**GATTTACT TTGTGCATA CAC**  
C27S  
CCTTATGATT ATAAAGAT**TG CAGGGT**AAAT TTTCAACGAC ACACACATT AAACATTGAT  
**GATT ATAAAGATTC CAGGGTAA**  
ACTCAAAAT ATAGAGGGAA AGACTATTAT ATTAGTTCCGA AATGTCTTA TGAGGCCTCT  
N79C  
CAAAAATTAA AACGAGATGA TCATGTAGAT GTTTTGGATT ATTTTATAT TCTT**ATATCT**  
**ATAT TCTTGTGT**  
CACACCGGTG AGTACATCTA TGGAGGAATT ACGCCTGCTCA AAATAATAA AGTAAATCAT  
**CA**  
AAATTATTGG GAAATCTATT TATTCGGGA GAATCTCAACA GAACTAAA TAACAAAATT  
ATTCTAGAAA AAGATATCGT AACTTCCAG GAAATTGACT TTAAAATCAG AAAATACCTT  
ATGGATAATT ATAAAATTAA TGACGCTACT TCTCCTTATG TAAGCGGCAG AATCGAAATT  
GGCACAAAAG ATGGGAAACA TGAGCAAATA GACTTATTTG ACTCACCAAA TGAAGGGACT  
**GAGGGACT**  
R181Q  
**AGATCAGATA TTTTGCAAA ATATAAGAT AATAGAATTA TCAATATGAA GAACTTTAGT**  
**CAATCAGATA TTTTGCA**  
CATTTCGATA TTTATCTTGAA (SEQ ID NO:3)

**Protein Sequence (combined mutants)**

DSKKDISNVK SDLLAAYTIT PYDYKDSRVN FSTTHTLNID TQKYRGKDYY ISSEMSYEAS  
QKFKRDDHVD VFGLFYILCS HTGEYIYGGI TPAQNNKVNH KLLGNLFISG ESQQNLNNKI  
ILEKDIVTFQ EIDFKIRKYL MDNYKIYDAT SPYVSGRIEI GTKDGKHEQI DLFDSPNEGT  
QSDIFAKYKD NRIINMKNFS HFDIYLE (SEQ ID NO:4)

Please amend the paragraph beginning at page 20, which starts with "The primary nucleotide", as follows:

The primary nucleotide sequence of truncated version of SPE-C is detailed below:

*DNA sequence (Factor X sequence shown in gray):*

GAC TCT AAG AAA GAC ATT TCG AAT GTT AAA AGT GAT TTA CTT TGC GCA TAC ACT  
ATA ACT CCT **ATC GAA CGT CGT** ACG CCT GCT CAA AAT AAT AAA GTA AAT CAT AAA  
TTA TTG GGA AAT CTA TTT ATT TCG GGA GAA TCT CAA CAG AAC TTA AAT AAC AAG  
ATT ATT CTA GAA AAG GAT ACC GTA ACT TTC CAG GAA ATT GAC TTT AAA ATC AGA  
AAA TAC CTT ATG GAT AAT TAT AAA ATT TAT GAC GCT ACT TCT CCT TAT GTA AGC  
GGC AGA ATC GAA ATT GGC ACA AAA GAT GGA AAA CAT GAG CAA ATA GAC TTA TTT

GAC TCA CCA AAT GAA GGG ACT AGA TCA GAT ATT TTT GCA AAA TAT AAA GAT AAT  
AGA ATT ATC AAT ATG AAG AAC TTT AGT CAT TTC GAT ATT TAT CTT GAA AAA TAA  
(SEQ ID NO:5)

*Protein Sequence*

D S K K D I S N V K S D L L C A Y T I T P **T E G R** T P A Q N N K V  
N H K L L G N L F I S G E S Q Q N L N N K I I L E K D T V T F Q E  
I D F K I R K Y L M D N Y K I Y D A T S P Y V S G R I E I G T K D  
G K H E Q I D L F D S P N E G T R S D I F A K Y K D N R I I N M K  
N F S H F D I Y L E K Stop (SEQ ID NO:6)

Please amend the paragraph beginning at page 21, which starts with "Synthetic peptide", as follows:

Synthetic peptide containing a C-terminal cysteine residue and SPEC-Y15A.C27S.N79C are mixed together and incubated at room temperature for 1 hour at a molar ratio of 1:2 in a alkaline buffer containing 1  $\mu$ M Cu<sup>2+</sup>. The copper acts as a redox catalyst. In the example below, a synthetic peptide of the pigeon cytochrome C (PCC) is provided, but this method will work for other peptides also so long as a free sulphur atom is present in the peptide.

SPEC- Y15A.C27S.N79C.R181 Q (MW 26,500) 10 mg/ml (380 $\mu$ M)	PCC peptide (RADLIAYLKQATKC) <u>(SEQ ID NO:21)</u> (MW 1400) 10 mg/ml (700 $\mu$ M)	Buffer
100 $\mu$ l	10 $\mu$ l	200mM Tris pH8.0, 1 $\mu$ M CuSO <sub>4</sub>

Please amend the paragraph beginning at page 22, which starts with "The 5C.C7 transgenic", as follows:

The 5C.C7 transgenic mouse was originally constructed by Berg et al.<sup>17</sup>. This mouse is transgenic for a TcR specific for the pigeon cytochrome C (PCC) peptide presented by mouse I-A<sup>d</sup>. Greater than 80% of mature T cells from 5C.C7 mice express the transgenic TcR and respond to synthetic PCC peptide RADLIAYLKQATK (SEQ ID NO:22) in vitro. This mouse

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provides an excellent means to test PCC specific T cell responses both in vitro and in vivo as well as conduct adoptive transfer experiments. Adoptive transfer is a powerful method that allows the introduction of PCC reactive T cells into non-transgenic mice to study responses at varying T cell precursor frequencies.